

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of :)
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 John P. Morseman, et al.) Group Art Unit: 1641
)
 Serial No.: 09/882,376) Examiner: Gary W. Counts
)
 Filed: June 18, 2001)
)
 For: HIGH FLUORESCENT)
 INTENSITY CROSS-LINKED)
 ALLOPHYCOCYANIN)

**SUBMISSION OF DECLARATION UNDER 37 C.F.R. §1.132 AND
CURRICULUM VITAE OF MARK WESLEY MOSS**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir,

Further to Applicants' Request for Continued Examination and Response filed herewith on March 1, 2005, Applicants submit a Declaration Under 37 C.F.R. §1.132 of inventor Mark Wesley Moss, together with a brief *Curriculum Vitae* [**Exhibit A**] for consideration. At the present time, Applicants are unable to provide the U.S. Patent and Trademark Office with an executed copy of the Declaration. Thus, Applicants respectfully request consideration of the Declaration without declarant Moss's signature. Applicants will submit an executed copy of the instant Declaration before March 4, 2005.

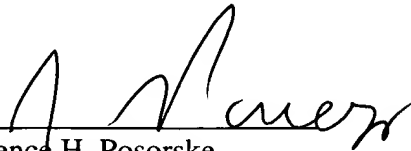
No fee is believed due in connection with this submission. However, if it is determined otherwise, the Patent Office is hereby authorized to charge any fees necessary or, to credit any overpayment to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

Hunton & Williams LLP

Dated: March 1, 2005

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: : MORSEMAN, et al. Confirmation No.: 6731
Application No.: : 09/882,376
Filed : June 18, 2001
Title : HIGH FLUORESCENT INTENSITY CROSS-LINKED
ALLOPHYCOCYANIN
TC/Art Unit : 1641
Examiner: : Counts, Gary W.

Docket No. : 62611.000202
Customer No. : 21967

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir,

I, Mark Wesley Moss, declare that:

1.) I attended The Johns Hopkins University from 1988 through 1992, in pursuit of a Bachelor of Sciences degree in Chemical Engineering.

2.) I have been associated with research in the field of immunoassay design and flow cytometry for approximately 14 years, and have co-authored several peer reviewed publications relating to the use of algal phycobiliproteins in various immunoassay applications, including flow cytometry. A recitation of some of these publications, together with details of my education, are given in the short version of my curriculum vitae, which is attached as **Exhibit A**. I have also developed phycobiliprotein-based reagents that are currently commercialized for use in applications such as flow cytometry and protein microarrays.

3.) I am a named inventor of U.S. Patent Application Serial Number 09/882,376 ("the '376 application").

4.) I understand that claims 3-14 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Park et al., *Homogenous Proximity Tyrosine Kinase Assays*, Anal. Biochem. 269: 94-104 (1999) ("the Park publication") in view of Applicants' prior sale of cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents ("Applicants' prior sale").

5.) I have read, and am familiar with, the following documents:

- a.) the '376 application;
- b.) the Park publication;
- c.) The Final Office Action issued by the United States Patent and Trademark Office ("the USPTO") in the '376 application on June 1, 2004;
- d.) The Advisory Action issued by the USPTO in the '376 application on October 4, 2004 ("the Advisory Action");
- e.) Applicants' Response to Final Rejection, filed September 1, 2004 ("Applicants' Response");
- f.) Nine (9) technical references describing flow cytometric assays ("the flow cytometry references") [Exhibit B], the abstracts of which were submitted with Applicants' Response; and
- g.) *Streptavidin and Fluorescent Conjugates of Streptavidin*, Molecular Probes, Product Information, 1-3 (August 2, 2004 revision) ("the Product Information") [Exhibit C].

6.) I understand that, during prosecution of the '376 application, the Examiner has taken the position that

Applicant provides nine (9) abstracts of papers . . . which describes the use of allophycocyanin in flow cytometric assays which do not involve time resolved fluorescence. These abstracts are not found persuasive because they are not clear on whether or not the allophycocyanin used in the assays is the native form of allophycocyanin or cross-linked allophycocyanin. . . . Applicant has not provided evidence to support the statements there is other known art uses for cross-linked allophycocyanin.

Advisory Action, pages 2-3 (emphasis in original).

7.) Based on my experience in the field of fluorescent specific binding assays, I have been asked to comment on whether the flow cytometry references **[Exhibit B]** represent an art-recognized use for cross-linked allophycocyanin that does not involve time-resolved fluorescence.

8.) Each of the nine flow cytometry references **[Exhibit B]** teaches the use of allophycocyanin, also referred to as "APC," in flow cytometric analyses. The flow cytometric assays described in the flow cytometry references are standard binding assays, in which fluorescence of bound labels is measured without any time-dependent gating. Thus, flow cytometric assays do not involve time-resolved fluorescence, and these nine references disclose use of allophycocyanin in a non-time-resolved manner.

9.) The allophycocyanin taught in each of the flow cytometry references **[Exhibit B]** is cross-linked allophycocyanin. For example, the Product Information states that the Molecular Probes' allophycocyanin used in various of the flow cytometry references is prepared from cross-linked allophycocyanin. See Product Information, page 2, column 1 **[Exhibit C]**. Five of the references in **Exhibit B** report using the Molecular Probes' allophycocyanin which is cross-linked.

10.) In addition, the Product Information confirms that the allophycocyanin used in such procedures is "chemically cross-linked . . . to avoid dissociation of the molecule into subunits when highly diluted." Product Information, page 2, column 1 **[Exhibit C]**. Flow cytometric procedures involve staining the cells to be analyzed, and the staining in the flow cytometry references is carried out with very dilute solutions of streptavidin-conjugated allophycocyanin. (2-20 ug/mL, see, e.g., the flow cytometry references (Beavis et al., *Detection of Cell-Surface Antigens Using Antibody-Conjugated Fluorospheres (ACF): Application for Six-Color Immunofluorescence*, BioTechniques 21: 498-503 (September 1996); Corver et al., *Four-Color Multiparameter DNA Flow Cytometric Method to Study Phenotypic Intratumor Heterogeneity in Cervical Cancer*, Cytometry 39: 96-107 (2000); Harding et al., *Using the Microcyte Flow Cytometer to Monitor Cell Number, Viability and Apoptosis in Mammalian Cell Culture*, Biotechnol. Prog. 16: 800-802 (2000); Schmid et al., *Measurement of Lymphocyte Subset Proliferation by Three-Color Immunofluorescence and*

DNA Flow Cytometry, J. Immun. Mthds. 235: 121-131 (2000)) [Exhibit B]). Therefore, I expect and believe that the allophycocyanin used in the four references that do not cite Molecular Probes as the source of allophycocyanin was cross-linked, because otherwise the molecule would have dissociated at the dilutions used in the procedure.

11.) Therefore, based on my experience and as further evidenced in the Product Information, each of the flow cytometry references [Exhibit B] teaches the use of cross-linked allophycocyanin in standard binding assays such as flow cytometric assays, which do not involve time-resolved fluorescence.

12.) Allophycocyanin conjugated to streptavidin is used for numerous procedures other than flow cytometry, including histochemistry, blot analysis and immunoassays. See Product Information, page 3, column 1 [Exhibit C]. These procedures do not involve time-resolved fluorescence. However, they do involve dilution of the allophycocyanin to concentrations similar to the concentrations in the flow cytometric assays. Thus, these procedures represent additional art-recognized uses for allophycocyanin where the molecule must be cross-linked to avoid dissociation.

13.) The undersigned acknowledges that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. § 1001), and may jeopardize the validity of the application or any patent issuing thereon. The undersigned declares further that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true.

Executed on _____

Declarant's Signature: _____

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